

CLAIMS:

1. (Original) A method of inducing or promoting dopaminergic neuronal development by enhancing proliferation, self-renewal, dopaminergic induction, survival, differentiation and/or maturation in a neural stem, progenitor or precursor cell, or other stem or neural cell, the method comprising:

expressing a nuclear receptor of the *Nurr1* subfamily above basal levels within the cell, and

treating the cell with a Wnt ligand, thereby producing or enhancing proliferation, self-renewal, survival and/or dopaminergic induction, differentiation, survival or acquisition of a neuronal dopaminergic phenotype.

2. (Original) A method according to claim 1 wherein the nuclear receptor is *Nurr1*.

3. (Original) A method according to claim 1 wherein the nuclear receptor is *Nor1* or NGFI-B.

4. (Currently amended) A method according to claim 1 ~~any one of the preceding claims~~ comprising expressing *Nurr1* above basal levels by transforming a cell with *Nurr1* DNA or introducing into the cell *Nurr1* RNA.

5. (Currently amended) A method according to claim 1 ~~any one of claims 1 to 3~~ comprising expressing *Nurr1* above basal levels by introducing *Nurr1* protein into the cell or by preserving *Nurr1* protein in the cell.

6. (Canceled)

7. (Currently amended) A method according to claim ~~any one~~ ~~of claims 1 to 6~~ wherein the Wnt ligand is selected from the group consisting of a Wnt1 ligand, a Wnt5a ligand, a Wnt3a ligand, a Wnt-2 ligand, a Wnt-4 ligand, a Wnt-7a ligand and a Wnt-7b ligand.

Claims 8-13 (Canceled)

14. (Currently amended) A method according to claim ~~any one~~ ~~of the preceding claims~~ wherein said neural stem, progenitor or precursor cell or other stem cell or neuronal cell is treated with Wnt ligands other than Wnt-1 or Wnt-5a or an additional Wnt ligand.

15. (Currently amended) A method according to claim ~~any one~~ ~~of the preceding claims~~ wherein the neural stem, progenitor or precursor cell or other stem or neural cell is mitotic and/or capable of self-renewal when it is treated with the Wnt ligand.

16. (Currently amended) A method according to claim ~~any one~~ ~~of the preceding claims~~ wherein said neural stem, progenitor or precursor cell or other stem or neural cell is additionally contacted with at least one of (i) a member of the FGF family of growth factors and (ii) at least one substance selected from the group consisting of a retinoid or retinoid derivative, an activator of the retinoid X receptor (RXR), a repressor of the retinoid acid receptor (RAR), 9-cis retinal, DHA, SR11237, or LG849.

17. (Canceled)

18. (Currently amended) A method according to claim 1~~any one of the preceding claims~~ wherein the neural stem, progenitor or precursor cell or other stem or neural cell is treated with bFGF and/or EGF and/or FGF-8 and/or LIF and/or Shh prior to or simultaneously with treating the cell with a Wnt ligand.

19. (Currently amended) A method according to claim 1~~any one of the preceding claims~~ wherein the neural stem, progenitor or precursor cell or other stem or neural cell is grown in the presence of antioxidants, ascorbic acid, low oxygen tension or a hypoxia-induced factor[[]].

20. (Currently amended) A method according to claim 1~~any one of the preceding claims~~ wherein the neural stem, progenitor or precursor cell or other stem or neural cell grows and/or differentiates in the presence of ventral mesencephalic astrocytes or early glial cells.

21. (Currently amended) A method according to claim 1~~any one of the claims 1 to 20~~ wherein the Wnt ligand is added to an in vitro culture containing the cell.

22. (Original) A method according to claim 21 wherein Wnt ligand is produced by expression from a cell co-cultured with the neural stem, progenitor or precursor cell, or other stem or neural cell, which co-cultured cell is a cell other than a type 1 astrocyte or early glial cell or is a host cell transformed with nucleic acid encoding the Wnt ligand or a cell containing introduced Wnt protein.

23. (Original) A method according to claim 22 wherein the co-cultured cell other than a type 1 astrocyte or early glial cell or host cell is another stem, neural stem, progenitor, precursor or neural cell.

24. (Original) A method according to claim 21 wherein the neural stem, progenitor or precursor cell, or other stem or neural cell, is engineered to express the Wnt ligand from encoding nucleic acid.

25. (Canceled)

26. (Currently amended) A method according to claim 1 ~~any one of claims 1 to 25~~ comprising further co-culturing the neural stem, progenitor or precursor cell, or other stem or neural cell, with an early glial cell, or a Type 1 astrocyte optionally of the ventral mesencephalon.

27. (Original) A method according to claim 26 wherein the Type 1 astrocyte is immortalized or is of an astrocyte cell line of a region other than the ventral mesencephalon.

28. (Currently amended) A method according to claim 1 ~~any one of the preceding claims~~, comprising additionally contacting the neural stem, progenitor or precursor cell, or other stem or neural cell with a negative selection agent that selects against non-dopaminergic neurons.

29. (Currently amended) A method according to claim 1 ~~any one of the preceding claims~~ further comprising formulating a neuron into a composition comprising one or more additional components, said composition optionally including a pharmaceutically acceptable excipient.

30. (Canceled)

31. (Currently amended) A method according to claim ~~30~~ 29 further comprising administering the composition to an individual.

32. (Original) A method according to claim 31 wherein the neuron is implanted into the brain of the individual.

Claims 33-39 (Canceled)

40. (Currently amended) A method according to claim 29 ~~any one of claims 31 to 39~~ wherein the individual has Parkinson's disease, a parkinsonian syndrome, neuronal loss or a neurodegenerative disease.

Claims 41-45 (Canceled)

46. (Currently amended) A method according to claim 1 ~~any one of claims 1 to 28~~ further comprising:

- (i) treating a dopaminergic neuron with a toxin for said dopaminergic neuron;

- (ii) separating the dopaminergic neuron from the toxin;

- (iii) bringing the treated dopaminergic neuron into contact with a test agent or test agents;

- (iv) determining the ability of the dopaminergic neuron to recover from the toxin;

- (v) comparing said ability of the dopaminergic neuron to recover from the toxin with the ability of a dopaminergic neuron to recover from the toxin in the absence of contact with the test agent or test agents.

47. (Currently amended) A method according to claim 1 ~~any one of claims 1 to 28~~ further comprising:

- (i) treating a dopaminergic neuron with a toxin for the dopaminergic neuron in the presence of a test agent or test agents;

- (ii) determining the ability of the dopaminergic neuron to tolerate the toxin;

(iii) comparing said ability of the dopaminergic neuron to tolerate the toxin with the ability of a dopaminergic neuron to tolerate the toxin in the absence of contact with the test agent or test agents.

Claims 48- 51 (Canceled)

52. (Original) A method of obtaining a factor or factors which, either alone or in combination, enhance proliferation, self-renewal, survival and/or dopaminergic development, induction, differentiation, or maturation in a neural stem, progenitor or precursor cell, or other stem or neural cell expressing *Nurr1* above basal levels, the method comprising:

(a) treating a neural stem progenitor or precursor cell, or other stem or neural cell expressing *Nurr1* above basal levels with a Wnt ligand in the presence and absence of one or more test substances; and

(b) determining proliferation, self-renewal, survival and/or dopaminergic development, induction, differentiation, or maturation of the cell and comparing the extent of the proliferation, self-renewal, survival and/or dopaminergic development, induction, differentiation or maturation in the presence and absence of the test substance or substances, whereby said factor or factors is obtained.

53. (Canceled)

54. (Original) A method according to claim 52, wherein the cell is treated with the Wnt ligand by introduction of nucleic acid encoding the Wnt ligand into the cell.

55. (Canceled)

56. (Currently amended) A method according to claim ~~52~~⁵³ wherein the neural stem, progenitor or precursor cell, or other stem or neural cell is treated with the Wnt ligand by co-culturing with a cell which is a cell other than a type 1 astrocyte or early glial cell or is a host cell transformed with nucleic acid encoding the Wnt ligand or a cell containing introduced Wnt protein, and said method optionally further comprises co-culturing the neural stem, progenitor or precursor cell, or other stem or neural cell with an early glial cell or a Type 1 astrocyte optionally of the ventral mesencephalon.

Claims 57-67 (Canceled)